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NOTE

EXPANDING ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE: A POLICY ANALYSIS AND LEGISLATIVE PROPOSAL

Austin Winniford[†]

I. INTRODUCTION

In early 2001, after a year and a half of increasingly ineffective chemotherapy treatments, 21 year old Abigail Burroughs ran out of FDA approved options for treating her head and neck cancer.¹ Abigail's oncologist at Johns Hopkins University told her and her father, Frank Burroughs, that there was a significant chance of saving Abigail's life if she could obtain the new cancer drug Erbitux, which was showing promising results in the clinical testing phase of development.² As early as 2000, there was compelling data that Erbitux was effective for treating head and neck cancer, including elimination of cancer in 87% of subjects in early clinical trials.³ Abigail did not qualify for a clinical trial because of the nature of her cancer, and despite significant efforts on behalf of her family, physician, and supporters over a seven-month period, she was unable to obtain Erbitux for use outside of a clinical trial.⁴ Abigail died in June of 2001.⁵ The

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¹ Complaint at 6-7, *Abigail Alliance v. Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007) (No. 04-5350).

² Sue Kovach, *The Abigail Alliance: Motivated by Tragic Circumstances, Families Battle an Uncaring Bureaucracy*, LIFE EXTENSION, Sept. 2007, at 26.

³ En Banc Brief of Appellants at 12-13, *Abigail Alliance v. von Eschenbach (Abigail II)*, 495 F.3d 695 (D.C. Cir. 2007) (No. 04-5350).

⁴ *Id.* at 9.

⁵ Complaint, *supra* note 1, at 7.

FDA approved Erbitux for the treatment of head and neck cancer five years later.⁶

In the 1990's, a high-dose chemotherapy plus autologous bone marrow transplant (HDC-ABMT) began showing promise in early clinical trials as a treatment for breast cancer.⁷ After intensive political lobbying, threats of litigation, and media involvement, insurance plans reluctantly agreed to cover the procedure, and more than 41,000 patients were able to obtain HDC-ABMT for treatment use outside of a clinical trial.⁸ Because of this expanded access, investigators struggled to enroll a sufficient number of patients in a later phase of clinical trials for HDC-ABMT, extending the testing process years longer than originally planned.⁹ Finally, after reports of many women dying from or being further disabled by this treatment, and after the cancer of the majority of women who received the treatment had regressed or progressed, randomized trial results indicated that HDC-ABMT offered no benefit over conventional treatment, with far greater toxicity.¹⁰

These cases illustrate the potential benefits and risks of expanding access to investigational drugs for treatment use and the flaws of the FDA regulations of such use. Although there is no data to support the claim, there is undoubtedly an unmet demand for investigational drugs outside of clinical trials.¹¹ For instance, more than 550,000 patients die from cancer every year in the United States,¹² and it is reasonable to assume that a significant proportion of these patients run out of effective approved treatment options at some point.¹³ Protocols for clinical trials typically contain limited space and restrictive qualification criteria regarding a patient's condition and treatment history; only 3% of cancer patients in the United States are enrolled in clinical trials.¹⁴ In most cases, qualification criteria exclude patients who have

⁶ En Banc Brief of Appellants, *supra* note 3, at 14.

⁷ Shira Bender et al., *Access for the Terminally Ill to Experimental Medical Innovations: A Three-Pronged Threat*, AM. J. BIOETHICS, Oct. 2007, at 3, 4.

⁸ *Id.*

⁹ Musa Mayer, *Listen to All the Voices: An Advocate's Perspective on Early Access to Investigational Therapies*, 3 CLINICAL TRIALS 149, 150 (2006).

¹⁰ *Id.*

¹¹ Telephone Interview with Michael Winniford, Dir. of Cardiology, Dir. of the Ctr. for Advanced Heart and Vascular Care, Professor and Vice Chair of the Departments of Med. and Surgery, Univ. of Miss. Med. Ctr. (Feb. 17, 2008).

¹² Manish Agrawal & Ezekiel J. Emanuel, *Ethics of Phase I Oncology Studies: Reexamining the Arguments and Data*, 290 JAMA 1075, 1075 (2003).

¹³ See Petition for Writ of Certiorari at 15, *Abigail Alliance v. von Eschenbach*, 2008 U.S. ___, 128 S. Ct. 1069 (Sept. 28, 2008) (No. 07-444).

¹⁴ Jerome Groopman, *The Right to a Trial*, NEW YORKER, Dec. 18, 2006, at 8.

received numerous treatments, patients with co-morbidities, and patients with recurrent cancer,¹⁵ yet these are often the patients in greatest need. In addition, for a variety of reasons, existing FDA mechanisms that allow patients to access investigational drugs outside of a clinical trial do not accommodate the demand.¹⁶ With a clinical testing process that lasts an average of seven years,¹⁷ the number of cancer patients who could benefit from obtaining investigational drugs outside of a clinical trial is potentially substantial. As the HDC-ABMT case illustrates, however, expanding access to investigational drugs risks harming patients by treating them with unproven, potentially toxic substances, and harming the public by undermining the integrity of clinical trials.

Despite the prominence of a recent court case¹⁸ and proposed federal legislation¹⁹ addressing these issues, the extent to which FDA regulations restrict access to investigational drugs and whether public policy supports these restrictions have not been thoroughly analyzed in the legal, health policy, bioethics, or medical literature. The majority of the relatively recent and few articles that defend a position on this issue briefly argue against expanding access to investigational drugs for treatment use.²⁰ In this paper I will defend a contrary posi-

¹⁵ See OVARIAN CANCER NATIONAL ALLIANCE, RESPONSE TO FOOD AND DRUG ADMINISTRATION RULE 21 CFR PART 312 (2007), available at <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06n-0062-EC57-Attach-1.pdf>.

¹⁶ Complaint, *supra* note 1, at 6.

¹⁷ *Id.* at 2.

¹⁸ *Abigail Alliance v. von Eschenbach (Abigail II)*, 495 F.3d 695 (D.C. Cir. 2007) (en banc).

¹⁹ See Access, Compassion, Care, and Ethics for Seriously Ill Patients Act (ACCESS Act), S. 1956, 109th Cong. (2005). See also CongressDaily, *Lawmakers To Reintroduce Bill Legalizing Terminally Ill Patients' Access To Experimental Medications*, MEDICAL NEWS TODAY, Aug. 21, 2007 (stating that representatives from both houses of Congress will likely reintroduce the ACCESS Act into the 110th Congress); National Cancer Act of 2007, S. 1056, 110th Cong. (2007) (directing the Secretary of Health and Human Services to establish a new program to expand access to investigational treatments for cancer patients who have exhausted all approved therapies).

²⁰ See, e.g., Bender et al., *supra* note 7; Mayer, *supra* note 9; George J. Annas, *Cancer and the Constitution – Choice at Life's End*, 357 NEW ENG. J. MED. 408 (2007); Peter D. Jacobsen & Wendy E. Parmet, *A New Era of Unapproved Drugs: The Case of Abigail Alliance v Von Eschenbach*, 297 JAMA 205, 208 (2007); Soc'y for Clinical Trials Bd. of Directors, *The Society for Clinical Trials Opposes US Legislation to Permit Marketing of Unproven Medical Therapies for Seriously Ill Patients*, 3 CLINICAL TRIALS 154, 155 (2006) ("[T]he approval process advocated in the Bill is not in the best interests of the patients."); O. Carter Snead, *Unenumerated Rights and the Limits of Analogy: A Critique of the Right to Medical Self-Defense*, 121 HARV. L. REV. 1 (2007), <http://harvardlawreview.org/forum/issues/120/may07/snead.pdf> (last visited Oct. 13, 2008); Arthur Caplan, *Is it Sound Public Policy to Let the Terminally*

tion and argue that FDA regulations of investigational drugs are overbroad in that they burden seriously and terminally ill patients with no approved treatment options more than necessary to further the government's interest in protecting patient safety and promoting public health. An unacceptable form of strong paternalism underlies FDA regulations in their role of restricting access to investigational drugs in order to protect the best interests of seriously and terminally ill patients. Moreover, Congress can enact legislation that eases the paternalistic restrictions on access without significantly jeopardizing patient safety or public health.

In Section II, I will summarize the recent effort to reform FDA regulations of investigational drugs through the judiciary in *Abigail Alliance v. Eschenbach*. Next, in Section III, I will outline the FDA's regulations of investigational drugs and elaborate on how they restrict access by discouraging industry involvement in expanded access programs. I describe the regulatory framework after I present the judicial issue in order to help the reader transition into Section IV, where I will assess whether the policies of protecting patient best interests and promoting public health justify the FDA's restrictions on access to investigational drugs. Concluding that they do not, in Section V, I will outline my recommendations for legislation that eases restrictions on access without undermining patient safety or public health. Finally, in Section VI, I will briefly evaluate the ACCESS Act, legislation currently before Congress that would substantially expand access to investigational drugs for treatment use.

II. INVESTIGATIONAL DRUGS AND THE CONSTITUTION

A. Case Background and the DC Circuit's Panel Decision

The Abigail Alliance for Better Access to Developmental Drugs (the Alliance) is a non-profit patient advocacy group formed in support of expanded access to investigational drugs. Abigail Burroughs' father, Frank Burroughs, formed the Alliance shortly after Abigail's death in 2001.²¹ In mid-2003, the Alliance and the Washington Legal Foundation sued the FDA Commissioner and the Secretary of the

Ill Access Experimental Medical Innovations?, AM. J. BIOETHICS, June 2007, at 1. But see John A. Robertson, *Controversial Medical Treatment and the Right to Health Care*, 36 HASTINGS CENTER REP. 15 (2006); Eugene Volokh, *Medical Self-Defense, Prohibited Experimental Therapies, and Payment for Organs*, 120 HARV. L. REV. 1813 (2007).

²¹ See Kovach, *supra* note 2 at 26.

Department of Health and Human Services, claiming that FDA policies violate the rights to privacy and liberty in the Constitution by interfering with the ability of Abigail Alliance patient-members and other terminally ill patients to make medical treatment decisions.²² Though not clear from the complaint or the opinions, the Alliance was specifically challenging two elements of the FDA's Treatment IND regulations, which govern access to investigational drugs for treatment use:²³ 1) the FDA's authority to deny access to an investigational drug for treatment use if it determines that the drug is not sufficiently safe or effective,²⁴ and 2) the requirement that drug sponsors may not charge more than cost recovery for an investigational drug,²⁵ which acts as a financial disincentive to making these drugs available outside of a clinical trial.

After a DC District Court dismissed the Alliance's complaint for failure to state a claim upon which relief could be granted,²⁶ a three-judge panel for the DC Circuit Court reversed.²⁷ The court held that terminally ill patients with no remaining approved treatment options have a constitutional right under the 14th Amendment's Due Process Clause to access post-Phase I investigational drugs, and remanded the case to the district court to determine whether FDA policies are narrowly tailored to further a compelling governmental interest.²⁸ In reaching its decision, the court applied the substantive due process framework articulated by the Supreme Court in *Washington v. Glucksberg*.²⁹ There, the Supreme Court upheld a Washington state law prohibiting assisted suicide by applying a three-part test for deriv-

²² Complaint, *supra* note 1, at 10.

²³ See *infra* Section III.A (describing the FDA's Treatment IND regulations).

²⁴ See, e.g., Petition for Writ of Certiorari, *supra* note 13, at 15 ("FDA policy is that [terminally ill patients who cannot get into a clinical trial] may seek access to the drug outside of the trial, and a willing drug company may provide it, *only* if they come to the FDA, fill out a mountain of regulatory paperwork, and convince FDA officials that the likely benefits outweigh the risks.").

²⁵ See, e.g., *id.* at 4 ("FDA regulations also forbid sponsors from 'charging a price larger than that necessary to recover costs of manufacture, research, development, and handling of the investigational drug.'") (quoting 21 C.F.R. § 312.7(d)(3)).

²⁶ Abigail Alliance v. McClellan, No. 03-1601, 2004 U.S. Dist. LEXIS 29594, at *36 (D.D.C., Aug. 30, 2004).

²⁷ Abigail Alliance v. von Eschenbach (*Abigail D*), 445 F.3d 470, 486 (D.C. Cir. 2006) ("[W]here there are no alternative government-approved treatment options, a terminally ill . . . patient's informed access to potentially life-saving . . . drugs determined by the FDA . . . to be sufficiently safe for expanded human trials warrants protection under the Due Process Clause."), *vacated*, 495 F.3d 695 (D.C. Cir. 2007).

²⁸ *Id.*

²⁹ *Washington v. Glucksberg*, 521 U.S. 702 (1997).

ing substantive due process rights under the 14th Amendment.³⁰ The Court required a “careful description” of the asserted constitutional right,³¹ required the right to be “deeply rooted” in America’s history and traditions,³² and required the right to be “implicit in the concept of ordered liberty.”³³

Although the nature of the “careful description” requirement is unclear, it is associated with a prohibition of deducing fundamental rights from more abstract concepts of personal autonomy.³⁴ In this respect, it is designed to emphasize judicial restraint by ensuring that judges frame the asserted right in a specific and narrow manner, and it appears to be similar to the method for framing an asserted right articulated by Justice Scalia in the plurality opinion for *Michael H. v. Gerald D.*³⁵ There, a biological father who had formed an intermittent relationship with his daughter filed an action to establish paternity and visitation rights.³⁶ His daughter was born out of wedlock after her mother, married to another man, had an affair with the plaintiff.³⁷ The Court framed the issue by asking whether society has traditionally protected the rights of the natural father of an adulterously conceived child, concluding that it has not.³⁸ Alternatively, in the dissent, Justice Brennan framed the issue by asking whether parenthood is a historically protected interest, concluding that it is.³⁹ In footnote six of the plurality opinion, Scalia explained his methodology by stating: “[w]e refer to the most specific level at which a relevant tradition protecting, or denying protection to, the asserted right can be identified.”⁴⁰ Notably, only Chief Justice Rehnquist joined Scalia on footnote six.⁴¹

After the careful description requirement, the second element in the *Glucksberg* test is that the asserted right must be “objectively, deeply rooted in this Nation’s history and tradition.”⁴² This element

³⁰ *Id.* at 722-36.

³¹ *Id.* at 721 (quoting *Reno v. Flores*, 507 U.S. 292, 302 (1993)).

³² *Id.* at 720-21 (quoting *Moore v. City of East Cleveland*, 431 U.S. 494, 503 (1977)).

³³ *Id.* at 721 (quoting *Palko v. Connecticut*, 302 U.S. 319, 325 (1937)).

³⁴ See *Abigail Alliance v. von Eschenbach (Abigail II)*, 495 F.3d 695, 707 n.13 (D.C. Cir. 2007) (en banc) (citing *Glucksberg*, 521 U.S. at 725).

³⁵ See John F. Basiak, Jr., *Inconsistent Levels of Generality in the Characterization of Unenumerated Fundamental Rights*, 16 J.L. & PUB. POL’Y 401, 418 (2005).

³⁶ *Michael H. v. Gerald D.*, 491 U.S. 110, 114 (1989).

³⁷ *Id.* at 113-14.

³⁸ *Id.* at 127 n.6.

³⁹ *Id.* at 137, 141-42, 145 (Brennan, J., dissenting).

⁴⁰ *Id.* at 127 n.6.

⁴¹ *Id.* at 113.

⁴² *Washington v. Glucksberg*, 521 U.S. 702, 720-21 (1997) (quoting *Moore*

also attempts to create judicial restraint by reducing subjectivity in substantive due process review. Third, fundamental rights must be “implicit in the concept of ordered liberty, such that neither liberty nor justice would exist if they were sacrificed.”⁴³ This element incorporates the notion that asserted rights should be morally important to individuals or society, in addition to being rooted in history, in order to be worthy of constitutional protection.⁴⁴ For example, although it is a national tradition to display fireworks on the 4th of July, this practice is likely not sufficiently integral to liberty or justice to warrant constitutional protection.⁴⁵

Applying these three elements, the circuit panel in *Abigail Alliance* “carefully” described the asserted right as “the right of terminally ill patients, acting on a doctor’s advice, to obtain potentially life-saving medication when no alternative treatment approved by the government is available.”⁴⁶ When inquiring whether this right is rooted in the nation’s history, however, the court strayed from its initial description, variously describing the right as “the right of control over one’s body[.]”⁴⁷ “the right to self-defense[.]”⁴⁸ “the right to self-preservation[.]”⁴⁹ “the right to act in order to save one’s own life[.]”⁵⁰ and the right “to assume any known or unknown risks of taking a medication that might prolong . . . life.”⁵¹ These alternative descriptions allowed the court to rely on the deep historical roots of certain common law rights, including the right to self-defense, in finding that the right asserted by the Alliance is rooted in national history and tradition.⁵² According to the court, where a terminally ill patient has exhausted all approved treatment options, government interference with his or her ability to access post-Phase I investigational drugs violates the right to self-defense or the right to self-preservation.⁵³

v. City of East Cleveland, 431 U.S. 494, 503 (1977)).

⁴³ *Id.* at 721 (quoting *Palko v. Connecticut*, 302 U.S. 319, 325 (1937)).

⁴⁴ See Roy G. Spece, Jr., *A Fundamental Constitutional Right of the Monied to “Buy Out Of” Universal Health Care Program Restrictions Versus the Moral Claim of Everyone Else to Decent Health Care: An Unremitting Paradox of Health Care Reform?*, 3 J. HEALTH & BIOMEDICINE 1, 78 (2007).

⁴⁵ *Id.*

⁴⁶ *Abigail Alliance v. von Eschenbach (Abigail I)*, 445 F.3d 470, 478 (D.C. Cir. 2006), *vacated*, 495 F.3d 695 (D.C. Cir. 2007).

⁴⁷ *Id.* at 480.

⁴⁸ *Id.*

⁴⁹ *Id.*

⁵⁰ *Id.* at 481 n.12.

⁵¹ *Id.* at 484.

⁵² *Id.* at 479-80 (“The absence of regulation could be attributable to a liberty interest that is deeply rooted in this Nation’s history and tradition. . . .”).

⁵³ *Id.* at 480.

The court also noted that regulating access to new drugs in the United States is a relatively recent phenomenon: prior to 1906, there was essentially no drug regulation in the United States, the government did not mandate testing for drug safety until 1938, and it did not mandate testing for drug efficacy until 1962.⁵⁴

Finally, the court determined that the right sought by the Alliance is implicit in the concept of ordered liberty, primarily because this conclusion is implied by the Supreme Court's decision in *Cruzan v. Missouri Dept. of Health*.⁵⁵ In *Cruzan*, although the Supreme Court affirmed Missouri's right to require clear and convincing evidence of an incompetent patient's wishes before withdrawing life-sustaining treatment, it assumed and strongly suggested that the Due Process Clause protects the right to refuse life-sustaining treatment.⁵⁶ The circuit court in *Abigail Alliance* analogized the right claimed by the Alliance to the right claimed in *Cruzan* by noting that neither right obligates the government to provide anything; both merely obligate the government not to interfere with a particular medical treatment decision.⁵⁷ In other words, both rights are negative rather than positive. The court then asserted that the same liberty interest that includes a right to refuse life-sustaining treatment must also include a right to access potentially life-sustaining medication.⁵⁸ Although the court did not make its reasoning transparent, the connection it established suggests that the Court in *Cruzan* derived the right to refuse life-sustaining treatment from a more general autonomy interest in making personally significant medical treatment decisions free from government interference. Thus, if the right to make medical treatment decisions resulting in death is significant enough to warrant constitutional protection, then the right to make medical treatment decisions that potentially prolong life should also be significant enough to warrant constitutional protection.

B. The DC Circuit's *En Banc* Decision

The DC Circuit vacated the panel's decision on November 21, 2006 and agreed to rehear the case *en banc*.⁵⁹ On August 7, 2007, the *en banc* court affirmed the initial decision of the district court, holding

⁵⁴ *Id.* at 481-82.

⁵⁵ *Id.* at 483-84.

⁵⁶ *Cruzan v. Dir., Mo. Dept. of Health*, 497 U.S. 261, 281 (1990).

⁵⁷ *Abigail I*, 445 F.3d at 484.

⁵⁸ *Id.* at 484-85.

⁵⁹ *Abigail Alliance v. von Eschenbach*, No. 04-5350, 2006 U.S. App. LEXIS 28974, at *1 (D.C. Cir. Nov. 21, 2006).

that the Due Process Clause does not protect the right sought by the Alliance and that the challenged FDA policy is rationally related to a legitimate state interest.⁶⁰ The court pointed out that the dissenting opinion, which was written by the same judge and is nearly identical to the vacated panel opinion, strays from the careful description requirement in its various broad descriptions of the right at issue.⁶¹ Nonetheless, the court directly addressed many of the dissent's arguments. In response to the panel's analogy to the common law right to self-defense, the court stated that the right to self-defense only justifies the use of a reasonable amount of force against an aggressor.⁶² According to the court, because the Alliance seeks a right to take drugs with significant risks and no proven therapeutic effect, taking an investigational drug prior to Phase II trials does not involve the use of reasonable force in self-defense.⁶³ The court also concluded that regulating drugs for safety and efficacy is deeply rooted in the history and traditions of the United States, citing numerous instances of drug regulation throughout the nation's history that the panel and dissent overlooked.⁶⁴ Moreover, the court noted that a mere failure to regulate does not indicate the existence of a fundamental right; it merely illustrates that Congress has responded to new risks presented by evolving technology.⁶⁵

Because the court concluded that a right to access investigational drugs is not deeply rooted in the nation's history, it did not decide whether this right is implicit in the concept of ordered liberty.⁶⁶ The court noted, however, that the Supreme Court in *Cruzan* based the right to refuse life-sustaining treatment on the common-law rule that forced medication is battery.⁶⁷ According to the court, because the Alliance does not seek freedom from forced medical treatment, the panel's analogy to *Cruzan* under the ordered liberty element was misguided. Concluding that the right claimed by the Alliance is not fundamental, the court then noted that unapproved, potentially toxic

⁶⁰ *Abigail Alliance v. von Eschenbach (Abigail II)*, 495 F.3d 695, 695, 713 (D.C. Cir. 2007) (en banc).

⁶¹ See *id.* at 701 n.5 (stating that the dissent recasts the proposed right away from the terms used in oral argument into a right "to try to save one's life" in tension with the careful description requirement).

⁶² *Id.* at 709-10.

⁶³ *Id.* But see Volokh, *supra* note 20 (defending use of investigational drugs by seriously and terminally ill patients with no approved treatment options as a legitimate exercise of the right to self-defense deserving constitutional protection).

⁶⁴ See *Abigail II*, 495 F.3d at 710-11.

⁶⁵ See *id.* at 711.

⁶⁶ *Id.* at 711 n.19.

⁶⁷ *Id.* at 712 n.19 (citations omitted).

drugs can harm even the terminally ill.⁶⁸ For example, these drugs may hasten their death or increase their suffering due to adverse side-effects. Thus, the court held that FDA regulations are rationally related to the legitimate state interest of protecting patients, including the terminally ill, from being harmed by unapproved drugs.⁶⁹

Although several Supreme Court cases are in tension, if not inconsistent with the careful description requirement and the associated prohibition of deducing rights from more abstract concepts related to personal autonomy,⁷⁰ the Supreme Court denied the Alliance's Petition for Writ of Certiorari on January 14, 2008.⁷¹ Apparently, the Court either did not perceive this tension or chose not to address it. In any event, the *Abigail Alliance* case illustrates that courts are not likely to protect a constitutional right to freedom from government interference with the pursuit of investigational medical treatment. Thus, proponents of expanded access to investigational drugs should pursue reform through legislation. The debate now shifts to Congress, where legislation such as the ACCESS Act threatens to change the regulatory framework governing investigational drugs.⁷²

⁶⁸ *Id.* at 713.

⁶⁹ *Id.*

⁷⁰ *See, e.g.,* *Roe v. Wade*, 410 U.S. 113, 153 (deducing the specific right to terminate a pregnancy from a broader right to privacy); *Griswold v. Connecticut*, 381 U.S. 479, 484-86 (deducing a specific right to use contraception from a broader right to be free from government intrusion into the marital bedroom); *Eisenstadt v. Baird* 405 U.S. 438, 453 (deducing a specific right to use contraception from a broader right to be free from governmental intrusion into matters so fundamentally affecting a person as the decision whether to have a child); *Planned Parenthood v. Casey*, 505 U.S. 833, 851 (1992) (suggesting that the 14th Amendment's conception of liberty encompasses "choices central to personal dignity and autonomy"); *Lawrence v. Texas*, 539 U.S. 558, 566-68 (overruling a decision that upheld a state law prohibiting sodomy because the Court previously framed the asserted right too narrowly, failing to appreciate the extent of liberty at stake). For discussion of these inconsistencies, *see generally*, Basiak, *supra* note 35; B. Jessie Hill, *The Constitutional Right to Make Medical Treatment Decisions: A Tale of Two Doctrines*, 86 Tex. L. Rev. 277, 281-82 (2007); Lee Goldman, *The Constitutional Right to Privacy*, 84 DENV. U. L. REV. 601 (2006); Brian Hawkins, Note, *The Glucksberg Renaissance: Substantive Due Process since Lawrence v. Texas*, 105 MICH. L. REV. 409 (2006).

⁷¹ Supreme Court of the United States Online Docket, Docket No. 07-444, <http://www.supremecourtus.gov/docket/07-444.htm> (last visited Sept. 26, 2008).

⁷² The ACCESS Act creates an auxiliary mechanism for drug approval that is designed to facilitate access to new drugs to seriously and terminally ill patients with no approved treatment options. Access, Compassion, Care, and Ethics for Seriously Ill Patients Act, S. 1956, 109th Cong. (2005). *See also* Section VI, *infra* (describing and evaluating the ACCESS Act).

III. FDA REGULATIONS OF INVESTIGATIONAL DRUGS

A. The Black-Letter Law

In 1938, Congress passed the Food, Drug, and Cosmetic Act (FDCA), prohibiting drug manufacturers from introducing a new drug into interstate commerce before it receives approval from the FDA.⁷³ In order to introduce a new drug, the drug's sponsor must first submit to the FDA an Investigational New Drug (IND) application, which includes results from animal and *in vitro* testing establishing that human testing is appropriate.⁷⁴ Next, the sponsor must conduct a series of clinical investigations to establish the safety and efficacy of the drug in human populations and submit the results to the FDA in a New Drug Application.⁷⁵ Pursuant to FDCA authority, the FDA has instituted a three-phase testing process.⁷⁶ Phase I trials introduce the new drug into the human population, typically involve 20 to 80 subjects, and are primarily designed to determine the drug's maximum tolerable dose and likely short-term side-effects.⁷⁷ Phase II trials typically involve several hundred subjects and are designed to evaluate the drug's effectiveness in treating a particular disease and to further evaluate the drug's short term side-effects.⁷⁸ Finally, Phase III trials are typically randomized and controlled, involve several thousand subjects and are designed to collect additional information about safety and effectiveness and to provide an adequate basis for labeling.⁷⁹ On average, the clinical trial process lasts seven years, and the entire drug development process costs the drug manufacturer nearly one billion dollars.⁸⁰

FDA exceptions to the standard approval procedures for new drugs fall into one of two categories: expedited review and expanded access. Expedited review involves expediting or shortening the review process and is not the subject of this paper. Expanded access

⁷³ 21 U.S.C. § 355(a) (2000).

⁷⁴ 21 C.F.R. § 312.23 (2008).

⁷⁵ 21 U.S.C. § 355(b)(1)(A) (2000).

⁷⁶ See 21 C.F.R. § 312.21 (2008).

⁷⁷ 21 C.F.R. § 312.21(a)(1) ("[Phase I] studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.").

⁷⁸ 21 C.F.R. § 312.21(b).

⁷⁹ 21 C.F.R. § 312.21(c).

⁸⁰ Groopman, *supra* note 14, at 2 (also noting that it typically takes 6.5 years for a drug manufacturer to gather enough data for IND testing approval).

involves providing access to investigational drugs for treatment use outside of a clinical trial. The primary mechanism for expanded access is the Treatment IND,⁸¹ also known as an expanded access protocol or a compassionate use protocol. In 1987, in response to political pressure from AIDS patients desperate for access to unapproved treatments, the FDA amended its IND regulations to include the Treatment IND.⁸² A Treatment IND allows a drug sponsor or investigator to develop a protocol primarily designed to treat a single patient or group of patients with an investigational drug.⁸³ The FDA will generally approve a Treatment IND for seriously ill patients as early as during Phase III trials, and for terminally ill patients as early as during Phase II trials, if the following conditions are met: 1) the drug is intended to treat a serious or immediately life-threatening disease; 2) there is no satisfactory treatment alternative for the intended patient population; 3) the drug is under investigation in a clinical trial or all trials have been completed; 4) the sponsor of the clinical trial is pursuing marketing approval with due diligence; and 5) there is sufficient evidence of safety and effectiveness to support using the drug for treatment.⁸⁴ Significantly, a sponsor, usually a pharmaceutical com-

⁸¹ The Parallel Track mechanism provides another means of expanded access, though specific to the treatment of AIDS and other HIV related diseases. Parallel Track studies run concurrently with traditional clinical investigations, but investigators conduct these studies without experimental controls, allowing patients who cannot gain entrance into a clinical trial to access the investigational drug. Peter M. Currie, *Restricting Access to unapproved Drugs: A Compelling Government Interest?*, 20 J.L. & HEALTH 309, 315 (2006/2007).

⁸² Groopman, *supra* note 14, at 3.

⁸³ 21 C.F.R. §§ 312.34(a)-35 (2008).

⁸⁴ 21 C.F.R. § 312.34(a)-(b) (not defining "serious" disease, and defining "immediately life-threatening" disease as "a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment."). The FDA's proposed regulations of investigational drugs for treatment use discuss the definition of "serious disease: "the 'serious disease or condition' requirement refers to conditions that have an important effect on functioning (e.g., stroke, schizophrenia, rheumatoid arthritis, osteoarthritis) or on other aspects of quality of life (e.g., chronic depression, seizures). Alzheimer's dementia, Amyotrophic Lateral Sclerosis (ALS), and narcolepsy are specific examples of serious conditions for which FDA has granted expanded access to investigational drugs in the past. Short-lived and self-limiting morbidity will usually not be sufficient to qualify a condition as serious, but the morbidity need not be irreversible, provided it is persistent or recurrent. Similarly, the proposed requirement here that treatment be for a "serious disease or condition" is not intended to be unnecessarily restrictive. It is primarily intended to exclude expanded access to investigational drugs for conditions that are clearly not serious (e.g., symptomatic relief of minor pain or allergic symptoms and other self-limiting conditions not associated with major morbidity). Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75147, 75151 (Dec. 14, 2006).

pany, may not “commercialize an investigational drug by charging a price larger than that necessary to recover costs of manufacture, research, development, and handling of the investigational drug.”⁸⁵

Likely responding to political pressure from the DC Circuit’s initial decision in *Abigail Alliance v. Eschenbach*, the FDA proposed regulations amending its current Treatment IND regulations in December of 2006.⁸⁶ According to the FDA, these proposed regulations are meant to clarify and codify, rather than change the agency’s existing regulations.⁸⁷ Indeed, the regulations themselves state that the FDA expects that “the overall impact of the proposed rule will not be significant.”⁸⁸ The only noteworthy revisions are the division of expanded access protocols into individual, small group and large group protocols, and the linking of the level of evidence required to support the use of an investigational drug with the number of patients likely to be treated.⁸⁹ In any event, as of writing this paper, the FDA has not adopted the proposed regulations. The following section illustrates that the consequences of maintaining the FDA’s current regulations are more adverse to access to investigational drugs than initially appears.

B. The Restrictive Implications of FDA Regulations for Access to Investigational Drugs

FDA regulations restrict access to investigational drugs for treatment use in several ways, some of which are not immediately apparent from the content of the regulations. First, it is apparent that the FDA will deny access if the drug is not intended to treat seriously or terminally ill patients, if the patients to be treated have an approved treatment option, or if the drug sponsor is not pursuing marketing approval through clinical trials with due diligence.⁹⁰ Libertarian views aside, these are relatively uncontroversial provisions that do not warrant further discussion. Second, the FDA will deny access if evidence indicates that the drug is not sufficiently safe or effective, and typically will not grant access prior to Phase II testing due to safety con-

⁸⁵ 21 C.F.R. § 312.7(d)(3) (2008).

⁸⁶ See Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75147.

⁸⁷ Corrected *En Banc* Brief for the Appellees at 12, *Abigail Alliance v. Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007) (No. 04-5350).

⁸⁸ Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75147, 75158 (Dec. 14, 2006).

⁸⁹ *Id.* at 75152-75155.

⁹⁰ See 21 C.F.R. § 312.34(a)-(b) (2008).

cerns.⁹¹ According to both the FDA and advocacy groups that support expanded access, however, these provisions are not the major obstacles to access.⁹² More importantly, drug sponsors, typically pharmaceutical companies, must voluntarily participate in Treatment IND's, and FDA regulations create several disincentives to sponsors making their investigational drugs available outside of a clinical trial.⁹³ The most significant disincentive is the provision prohibiting sponsors from charging a profit-making price for investigational drugs for treatment use.⁹⁴ Like any corporation, the profit-motive dictates the conduct of pharmaceutical companies. Only allowing these companies to recover the costs of making investigational drugs available outside of a clinical trial does not even constitute compensation for total expenses, because it excludes opportunity costs associated with time, effort and inconvenience.

FDA regulations also create disincentives to making investigational drugs available outside of clinical trials for reasons related to the collection of data for marketing approval. The FDA has not tradi-

⁹¹ See 21 C.F.R. 312.34(a), 312.34(b)(3).

⁹² See Corrected *En Banc* Brief for the Appellees, *supra* note 87, at 14 (stating that the FDA approves most of the single-patient Treatment IND requests submitted); Huntington's Disease Drug Works et al., A Written Comment Submitted to the FDA (2007), <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06n-0062-EC27-Attach-1.pdf> (stating that lack of industry support is by far the most significant problem for expanded access programs); Jeff Ryan, *Advocates for Patient Rights Want 'Initial Approval' for Unproven Drugs*, APPLIED CLINICAL TRIALS, May 1, 2004, (interviewing Frank Burroughs, founder of the Abigail Alliance for Better Access to Developmental Drugs, who states that the Treatment IND program has not worked because of regulatory disincentives and a lack of reasonable economic incentives).

⁹³ See Beryl Lieff Benderly, *Experimental Drugs on Trial*, SCI. AM., Oct. 2007, at 93, 95-96 (quoting Scott Gottlieb, a former FDA deputy commissioner for medical and scientific affairs, for the proposition that "[t]he biggest impediment [to early access to investigational drugs outside of trials] is the unwillingness of some companies to offer the drug.") (second alteration in original); Annas, *supra* note 20, at 411 (claiming that the FDA's proposed regulations of investigational drugs will do little to increase access because manufacturers have no incentives to make their investigational products available outside clinical trials).

⁹⁴ See, e.g., Vital Therapies, A Written Comment Submitted to the FDA (Jan. 30, 2007), <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06n-0062-c000005-01-voll.pdf> (stating that the FDA's proposed regulations on charging for investigational drugs are restrictive because they do not provide a financial incentive to make investigational drugs available); Huntington's Disease Drug Works et al., *supra* note 92 (suggesting that the FDA can address the problem of limited access to investigational drugs by offering financial incentives to industry companies); Complaint, *supra* note 1, at 6 (suggesting that compassionate use programs are too small because drug sponsors may not charge more than a cost recovery amount to participants).

tionally allowed efficacy information gained from expanded access protocols to be included as evidence in a New Drug Application.⁹⁵ In this respect, data from expanded access protocols does not support the goal of market approval and cannot benefit the company. Moreover, anecdotal evidence associated with an adverse reaction to an investigational drug in an uncontrolled setting might raise safety concerns that could hinder market approval or create adverse publicity.⁹⁶ Thus, drug companies may bear costs associated with negative outcomes in an expanded access setting, while they cannot benefit from positive outcomes.

Liability concerns are additional disincentive to participating in expanded access programs. According to Eli Lilly, one of the world's largest pharmaceutical companies, FDA approval of an expanded access protocol does not remove investigator and sponsor liability for an adverse event as a concern.⁹⁷ Indeed, pharmaceutical companies could be held liable for injuries in this context based on theories of strict products liability, failure to warn, negligence, or fraud.⁹⁸ Although FDA regulations do not *create* concerns over liability, they do not offer any protection against it. Regardless of whether this is good policy, the prospect of getting sued creates an additional disincentive to making investigational drugs available for treatment use.

Physicians also face disincentives and obstacles to obtaining investigational drugs in order to treat their patients. Many physicians find the administrative hassle and time commitment associated with requesting these drugs so burdensome that they do not even attempt to obtain them.⁹⁹ While this may sound callous, for most physicians,

⁹⁵ GLAXOSMITHKLINE, RE: DOCKET NO. 2006N-002 (RIN 0910-AF14): COMMENTS ON THE PROPOSED RULE ON "EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE" (FEDERAL REGISTER 71: 75147-75168, DECEMBER 14, 2006) (2007), available at <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06N-0062-EC87-Attach-1.pdf>.

⁹⁶ Groopman, *supra* note 14, at 7; Currie, *supra* note 81, at 322-323.

⁹⁷ ELI LILLY AND COMPANY, COMMENTS ON FEDERAL REGISTER NOTICE: PROPOSED RULE: EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE: DOCKET NO. 2006N-0062 (2007), available at <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06N-0062-EC53-Attach-1.pdf>. See also Groopman, *supra* note 14, at 4 (stating that drug companies are reluctant to supply experimental drugs outside of a clinical trial in part because of the fear that patients who suffer adverse reactions will sue the company).

⁹⁸ Meghan K. Talbott, *The Implications of Expanding Access to Unapproved Drugs*, 35 J. L. MED. & ETHICS 316, 318 (2007).

⁹⁹ Telephone Interview with Michael Winniford, *supra* note 11. See also Ellen Stovall et al., A Written Comment Submitted to the FDA (Mar. 14, 2007), <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06N-0062-EC91-Attach-1.pdf> ("many physicians find the process of applying for individual access to be un-

practicing in the current high-demand environment is impossible without rationing time and responsibilities to a certain extent.¹⁰⁰ Adding to the problem, many physicians simply are not aware of the existence of investigational drugs that could benefit their patients.¹⁰¹ Although Congress mandated registry of all clinical trials relevant to serious or life threatening diseases on the public database ClinicalTrials.gov in the Food and Drug Administration Modernization Act of 1997,¹⁰² there are no enforcement mechanisms and lack of compliance is evident.¹⁰³

In light of these obstacles and disincentives, it may seem surprising that access to investigational drugs outside of clinical trials does in fact occur.¹⁰⁴ The most plausible explanation for this is that drug companies have an incentive to promote a positive reputation among physicians and other health care providers.¹⁰⁵ Physicians tend to respond favorably to drug companies that appear to have patient best interests in mind by participating in indigent drug programs or expanded access protocols.¹⁰⁶ Ultimately, drug companies hope that this positive image will affect physicians' prescription patterns and translate to revenue for the company. Some companies may determine that these potential revenues offset any costs or lack of benefit associated with making their investigational drugs available for treatment use. However, many drug companies know which physicians have the greatest influence within the medical community.¹⁰⁷ The incentive to promote a positive image may only be strong enough to induce companies to expand access in the relatively rare transactions involving these influential physicians.¹⁰⁸ Undoubtedly, access to investigational drugs for treatment use has been concentrated in academic medical settings in part because influencing a prominent teacher has an even greater potential multiplier effect.¹⁰⁹ Thus, despite the incentive to

duly burdensome"); Huntington's Disease Drug Works et al., *supra* note 92 ("the process [of obtaining an investigational drug for a desiring patient] remains so labor intensive that very few individual physicians can afford the time and expense").

¹⁰⁰ Telephone Interview with Michael Winniford, *supra* note 11.

¹⁰¹ Telephone Interview with Michael Winniford, *supra* note 11.

¹⁰² See Jennifer L. Gold & David M. Studdert, *Clinical Trials Registries: A Reform that Is Past Due*, 33 J.L. MED. & ETHICS 811, 815 (2005).

¹⁰³ *Id.* at 816.

¹⁰⁴ There is no helpful data indicating how often such access occurs.

¹⁰⁵ Telephone Interview with Michael Winniford, *supra* note 11.

¹⁰⁶ *Id.*

¹⁰⁷ *Id.*

¹⁰⁸ *Id.*

¹⁰⁹ See Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75147, 75149 (Dec. 14, 2006) (expressing concern over claim that patients treated outside of academic medical centers are less likely to have access to investiga-

influence physicians, FDA regulations in collaboration with industry disincentives still almost certainly ensure that supply does not come close to meeting the demand for investigational drugs. Ultimately, whether Congress should require the FDA to relax these restrictions on access depends on the soundness of the policy justifications supporting them.

IV. THE POLICY BEHIND REGULATING INVESTIGATIONAL DRUGS FOR TREATMENT USE

Determining whether Congress should direct the FDA to reform its investigational drug regulations is a policy judgment involving the balancing of competing interests. On the one hand, seriously and terminally ill patients with no remaining approved treatment options should be able to access potentially beneficial yet unapproved drugs. On the other hand, restricting access to unapproved drugs furthers the government's legitimate interest in protecting patients and promoting public health. In this section and the following section I will argue that FDA regulations do not strike the appropriate balance because they unduly favor the latter interests at the expense of the former. I will evaluate the primary governmental interests that justify restrictions on access to investigational drugs: protecting seriously and terminally ill patients from the consequences of their own decision to take a potentially dangerous and unproven drug, promoting public health by ensuring the efficiency and integrity of clinical trials, and promoting public health by preventing the widening of health disparities.¹¹⁰ I will argue that an unacceptable form of strong paternalism underlies FDA regulations in their role of restricting access to investigational drugs in order to protect patient best interests. I will also argue that FDA regulations are overbroad and that Congress can relax the strongly paternalistic restrictions on access to investigational drugs without significantly jeopardizing patient safety or public health.

tional drugs for treatment use).

¹¹⁰ In dividing my policy analysis into the government's interest in protecting the best interests of patients on the one hand and promoting public health on the other hand, I consider future patients under the rubric of public health. As already evident, I devote my analysis of patient best interests in this section to the best interests of the seriously and terminally ill patients with no approved treatment options who would be eligible to take investigational drugs.

A. Regulating Investigational Drugs to Protect Seriously and Terminally Ill Patients from Their Own Decisions

In some cases, the government has a legitimate interest in protecting its citizens from the harmful consequences of their own decisions, even where these consequences fall primarily on the decision-maker. Such protection is particularly justified in health care, where disease often impairs consumer capacity, considerable informational asymmetries exist between provider and consumer, and decisions are often crucial to well-being. For example, courts may grant physicians the legal authority to disregard a patient's medical treatment decision and force unwanted treatment where a physician determines that a patient does not have the capacity to make the requisite decision.¹¹¹ This type of legal interference with a personal decision is justified because incompetent individuals no longer tend to make decisions that promote their best interests as determined by their own values. However, assuming the decision is primarily self-regarding, or in other words that any adverse effects of the decision do not fall substantially on others,¹¹² the government should not intervene to protect competent patients from the consequences of their own medical treatment decisions. This conclusion assumes that competent patients make decisions that promote their own values, and thus intervening is not in their best interests. The only alternative assumption is that the policies behind government intervention are more in accord with a competent patient's best interests than the patient's own values, which is the assumption underlying strong paternalism. In a liberal society that protects a plurality of the good such as the United States, regulations that tend towards strong paternalism are rarely, if ever, good policy.

1. The Arguments for Justifying FDA Restrictions Based on the Best Interests of Seriously and Terminally Ill Patients

In holding that FDA regulations are rationally related to the legitimate state interest of protecting terminally ill patients from being harmed by unapproved drugs, the DC Circuit in *Abigail Alliance* appealed to patient best interests as a justification for the FDA's policies.¹¹³ In its brief, the FDA echoed this justification, stating: "By

¹¹¹ See, e.g., KY. REV. STAT. ANN. § 202A.196 (LexisNexis 2008) (establishing the conditions under which district courts can authorize forced treatment of the mentally ill).

¹¹² I make this assumption for the purposes of this section because I address the potential adverse effects on others of a decision to take an investigational drug in Section IV:B, *infra*.

¹¹³ See *Abigail Alliance v. von Eschenbach (Abigail II)*, 495 F.3d 695, 713

acting as a regulatory gatekeeper, the FDA increases the likelihood that the use of an investigational drug will further the underlying interests in life and health that the patient's choice is intended to advance."¹¹⁴

Indeed, there are *prima facie* plausible arguments for patient best interests as a justification for the FDA's proscription of a market for investigational drugs. As an initial matter, the dangers of investigational drugs indirectly support this justification. Especially in the early phases of testing, investigational drugs *are* unsafe and ineffective relative to approved drugs.¹¹⁵ By hastening death or increasing suffering, these relatively unsafe and ineffective drugs can harm even the terminally ill. To be sure, even where risk is extremely high, interfering with a competent patient's substantially self-regarding medical treatment decision remains based in strong paternalism. After all, competent patients in collaboration with their physicians are in a better position to determine their own aversion to risk and make their own risk-benefit assessments than anyone else, including the FDA. However, some bioethicists and clinicians have proposed models for determining competence that account for risk levels, known as sliding-scale models of competence.¹¹⁶ Under a sliding-scale model, the level of evidence required to determine competence increases with the risk associated with a particular decision.¹¹⁷ These models accommodate the intuition that the importance of ensuring that an individual possesses the requisite capacities increases with the magnitude and risk of harm associated with a particular decision.¹¹⁸ For example, it seems reasonable to require more of evidence indicating competence for a decision to refuse a simple but life-saving blood transfusion than for a decision to accept the same transfusion. Thus, under a sliding-scale model, deciding to take a relatively unsafe investigational drug would impose a high evidentiary burden for competence on seriously and terminally ill patients. The argument could proceed with the

(D.C. Cir. 2007) (en banc).

¹¹⁴ Corrected *En Banc* Brief for the Appellees, *supra* note 87, at 23.

¹¹⁵ I further discuss the safety and effectiveness of investigational drugs in Section IV:A:2, *infra*.

¹¹⁶ See e.g., THOMAS GRISSO & PAUL S. APPELBAUM, *ASSESSING COMPETENCE TO CONSENT TO TREATMENT* 139 (Oxford Univ. Press 1998); ALLEN E. BUCHANAN & DAN W. BROCK, *DECIDING FOR OTHERS: THE ETHICS OF SURROGATE DECISION MAKING* 51-70 (1990); TOM L. BEAUCHAMP & JAMES F. CHILDRESS, *PRINCIPLES OF BIOMEDICAL ETHICS* 74-77 (Oxford Univ. Press 5th ed. 2001). For discussion and criticisms of sliding-scale models, see Mark R. Wicclair, *The Continuing Debate over Risk-Related Standards of Competence*, 13 *BIOETHICS* 149 (1999).

¹¹⁷ BEAUCHAMP ET AL., *supra* note 116, at 76.

¹¹⁸ *Id.* at 75.

claim that the decision to take one of these drugs made by a seriously or terminally ill patient is not likely to meet this high evidentiary burden.

The primary basis for challenging competence in this context is the prejudicial effect of serious or terminal illness on voluntariness. Critics of expanded access claim that the desperation associated with serious illness inhibits or prevents patients from accurately understanding or assessing the risks and benefits of a decision to take an investigational drug.¹¹⁹ This conclusion is largely based on the notion that desperate patients are particularly vulnerable to the unrealistic belief that unproven treatment will benefit them, also known as the therapeutic misconception.¹²⁰ In fact, bioethicist and law professor George Annas has characterized the terminally ill as "the most vulnerable research subject," claiming that research rules should disqualify all desperate patients from participating in research.¹²¹ Furthermore, some commentators appeal to the "coercive" influence of the therapeutic misconception on desperate patients,¹²² which implies that unrealistic hope narrows a patient's options to the extent that he or she is effectively forced to make a harmful decision.¹²³

¹¹⁹ See e.g., Corrected *En Banc* Brief for the Appellees, *supra* note 87, at 50 ("[D]esperation...has the inescapable potential to prevent an accurate evaluation of the risks and benefits of experimental drugs"); Caplan, *supra* note 20, at 2 ("Nor is it clear that those who are terminally ill can make the requisite autonomous risk/benefit decision to use a new drug . . .").

¹²⁰ See Caplan, *supra* note 20, at 2 ("The desire to hope for the best – what is sometimes termed the therapeutic misconception – is often present on the part of those facing death . . ."); Andrew F. Shorr, *AIDS and the FDA: An Ethical Case for Limiting Patient Access to New Medical Therapies*, IRB: ETHICS & HUM. RES., July-Aug. 1992, at 1, 3 ("Patients desperately seeking cure who enter a study that offers only hope . . . are hardly capable of granting informed consent in a fully voluntary manner.") (quoting Ruth Macklin & Gerald Friedland, *AIDS Research: The Ethics of Clinical Trials*, 14 L. MED. & HEALTH CARE 273, 279 (1986)); Annas, *supra* note 20, at 412 (stating that the *Abigail Alliance* court that held that there is a fundamental right to certain investigational drugs seems to be suffering from a therapeutic illusion in which research is confused with treatment).

¹²¹ George J. Annas, *The Changing Landscape of Human Experimentation: Nuremberg, Helsinki, and Beyond*, 2 HEALTH MATRIX 119, 120, 135 (1992).

¹²² JESSICA W. BERG ET AL., INFORMED CONSENT: LEGAL THEORY AND CLINICAL PRACTICE 68 (2nd ed. 2001) ("Physicians should be aware of how vulnerable patients may be to the coercive influence of unrealistic hope, especially those suffering from chronic, life-threatening disorders").

¹²³ See Jennifer S. Hawkins & Ezekiel J. Emanuel, *Clarifying Confusions about Coercion*, 35 HASTINGS CENTER REP. 16, 17 (defining coercion as the unfavorable narrowing of a person's choices in order to get the person to do something he would not otherwise do).

In addition, some critics of expanded access challenge competence in this context by arguing that it is difficult or impossible to adequately inform patients about the risks and benefits of an investigational drug where so little data is available, especially in the early phases of testing.¹²⁴ Typically, data from Phase I trials only pertains to 20 to 80 subjects and to maximum tolerable dose and likely short-term side effects.¹²⁵ This simply may not be enough information to understand the consequences of a decision to take a drug early in the testing process, and a decision made without understanding the consequences is not competent. In sum, if these threats to the competence of a seriously or terminally ill patient's decision to take an investigational drug are legitimate and substantial, FDA restrictions are in patients' best interests.

A separate set of considerations linking FDA restrictions to the best interests of seriously and terminally ill patients specifically relates to the prospect of allowing drug companies to charge a profit-making price for investigational drugs. Namely, doing so puts them in a position to exploit the desperation of these patients through price gouging and manipulative marketing.¹²⁶ Price gouging occurs when a seller takes advantage of an unusually high demand and lack of competition by charging excessively high prices.¹²⁷ Price gouging is especially worrisome in a critical healthcare context: desperate patients facing death who have sufficient means may be willing to pay exorbitant prices for one last chance at curing or ameliorating their illness. In addition, allowing profit creates incentive to advertise, and drug marketers could undoubtedly devise subtle ways to capitalize on desperation through advertising. Prohibiting drug companies from profiting from investigational drugs ensures that neither of these practices will occur and thereby protects the best interests of patients.¹²⁸

¹²⁴ See Annas, *supra* note 20, at 412; *Abigail Alliance v. von Eschenbach (Abigail D)*, 445 F.3d 470, 496 (D.C. Cir. 2006) (Griffith, J., dissenting) (quoting the FDA), *vacated*, 495 F.3d 695 (D.C. Cir. 2007).

¹²⁵ 21 C.F.R. § 312.21(a) (2008). Increasingly, however, Phase I oncology trials test for therapeutic benefit, usually as a secondary endpoint. Thomas G. Roberts et al., *Trends in the Risks and Benefits to Patients With Cancer Participating in Phase I Clinical Trials*, 292 JAMA 2130, 2131 (2004).

¹²⁶ See Annas, *supra* note 121, at 132-133 (stating that pharmaceutical companies can make money by exploiting fear of death and desperation).

¹²⁷ See Michael Brewer, Note, *Planning Disaster: Price Gouging Statutes and the Shortages They Create*, 72 BROOK. L. REV. 1101, 1101 (2007).

¹²⁸ Because my response to these arguments comes in the form of recommendations for legislation, I defer it to Section V:A, *infra*.

2. Responding to Arguments that Appeal to the Best Interests of Seriously and Terminally Ill Patients

Upon closer examination, many of the concerns about the safety and effectiveness of investigational drugs and the competence of a decision to take them are overstated or misguided. Focusing on the safety and effectiveness of investigational oncology treatments, for years the most commonly cited figures indicated that Phase I trials of anti-cancer drugs led to an overall response rate of about 5% and a rate of death from toxic effects of 0.5% or lower.¹²⁹ (Overall response rate represents the sum of the complete response rate – a complete disappearance of a tumor – and the partial response rate – a 50% or greater reduction in the size of the tumor).¹³⁰ Presumably, these are some of the figures that the FDA would have used in assessing the risks and benefits of investigational drugs to help design its Treatment IND program in 1987. But in addition to being outdated, these figures are misleading. Of the studies reporting these response rates, the latest available analysis reports on trials published from 1970-1987, failing to account for trials done with newer compounds¹³¹ or trials done with a combination of agents.¹³² Newer compounds may lead to more favorable response rates because researchers are increasingly able to design drugs that target the root causes of disease.¹³³ Furthermore, because all subjects must have progressive cancer to qualify for a Phase I oncology trial,¹³⁴ the absence of data indicating less-than-partial responses and stabilization of disease betrays the overall effect of these trials. In other words, in order to present a complete perspective, studies involving patients whose cancer is growing or spreading should account for less than 50% tumor shrinkage and lack of tumor growth.

In light of these shortcomings, Horstmann et al. conducted a more comprehensive study using data from 460 Phase I oncology trials

¹²⁹ Elizabeth Horstmann et al., *Risks and Benefits of Phase I Oncology Trials, 1991 through 2002*, 352 NEW ENG. J. MED. 895, 901 (2005) (citing nine different studies that support these figures); see also Agrawal et al., *supra* note 12, at 1075-76 (citing four different studies that support the data on response rate and one study that supports the data on toxicity related death).

¹³⁰ Horstmann et al., *supra* note 129, at 897.

¹³¹ Agrawal et al., *supra* note 12, at 1076.

¹³² Horstmann et al., *supra* note 129, at 896.

¹³³ See Roberts et al., *supra* note 125, at 2130 (stating that the risk-benefit ratio of Phase I oncology trials may have improved in part because of the targeted and less toxic nature of newer cancer drugs).

¹³⁴ Razelle Kurzrock & Robert S. Benjamin, *Risks and Benefits of Phase I Oncology Trials, Revisited*, 352 NEW ENG. J. MED. 930, 930 (2005).

involving 11,935 subjects between 1991 and 2002.¹³⁵ The results indicated an overall response rate of 10.6%, a stable disease or a less-than partial response rate of 34.1%, and a toxicity related death rate of .49%.¹³⁶ Interpreting the results, 44.7% of subjects derived a physiological benefit in terms of tumor shrinkage or lack of growth from the trials analyzed.¹³⁷ Granted, these results do not necessarily reflect an increase in quality of life because they do not indicate response duration, which refers to the length of time for which a drug reduces the size of a tumor, and because they do not account for the impact of potential side-effects.¹³⁸ But this study does provide important evidence that investigational oncology drugs are increasingly effective at reducing or stabilizing tumors early in the testing process.¹³⁹ In fact, the response rates observed in these Phase I oncology studies are not clearly worse than response rates used by the FDA as a basis for approval of certain cancer treatments.¹⁴⁰ For example, high-dose interleukin 2, the only FDA-approved treatment for metastatic renal cell carcinoma, has a response rate of 14%.¹⁴¹ In addition, the FDA approved topotecan for ovarian cancer, which has a 10% response rate, and gemcitabine for metastatic pancreatic cancer, which has a 5.4% response rate.¹⁴²

Moreover, in some cases response rates to investigational oncology treatments are extremely high. For example, a Phase I trial of imatinib mesylate for chronic leukemia resulted in a 93% response rate.¹⁴³ In addition, monoclonal antibody IMC-C225, plus radiation therapy, led to a complete response rate of 87% in patients with locally advanced, inoperable head and neck cancers.¹⁴⁴ Where a major subset of early-stage investigational drugs now demonstrate

¹³⁵ Horstmann et al., *supra* note 129, at 898-99.

¹³⁶ *Id.* at 895.

¹³⁷ See Kurzrock et al., *supra* note 134, at 930.

¹³⁸ The overall frequency, severity, and impact on quality of life of nausea, vomiting, and other debilitating adverse effects from cancer treatments have been poorly documented. Agrawal et al., *supra* note 12, at 1077.

¹³⁹ Note that the data presented here applies to results from clinical trials. Results from outside of a clinical trial setting would likely vary slightly due to differences between research and treatment settings in average patient condition and the nature and level of care.

¹⁴⁰ Agrawal et al., *supra* note 12, at 1077.

¹⁴¹ *Id.*

¹⁴² *Id.*

¹⁴³ Kurzrock et al., *supra* note 134, at 931.

¹⁴⁴ Am. Cancer Soc'y, *Monoclonal Antibody Drug IMC-C225 Shows Wide Promise*, ACS NEWS CENTER, May 24, 2000, http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Monoclonal_Antibody_Drug_IMC_C225_Shows_Wide_Promise.asp.

response rates comparable to certain approved treatments, and occasional response rates well above many approved treatments, justifying regulations that deny patients with no other options access to these drugs by appealing to their own good begins to seem questionable. Furthermore, average response rates to Phase II and Phase III drugs can only be higher and as indicated, response rates to all investigational drugs will likely increase as researchers learn more about the root causes of disease and develop drugs that target these root causes.¹⁴⁵ The FDA has not significantly revised its expanded access regulations in twenty-one years and should respond to these advancements in technology.

While these considerations primarily apply to effectiveness, there is also reason to believe that investigational drugs are not exceedingly unsafe for seriously or terminally ill patients with no approved treatment options. Investigational drugs are not quackery: in order for an IND Application to receive approval, the FDA must assess data from animal and *in vitro* studies and determine that it is "reasonably safe to conduct the proposed clinical investigations" in a human population.¹⁴⁶ One study reported that the FDA ultimately approves only 11% of all drugs that enter into clinical testing.¹⁴⁷ However, even though it is difficult to collect accurate data in this context because researchers do not always disclose unfavorable data,¹⁴⁸ this figure alone is misleading. Sponsors do not always abandon drugs for safety-related reasons. For example, one study analyzed clinical trials for all drugs from 1981-1992 and found that sponsor abandonment occurred for safety reasons only 20.5% of the time.¹⁴⁹ Lack of efficacy or economic concerns accounted for most instances of abandonment.¹⁵⁰

Perhaps more importantly, however, critics of expanded access who appeal to the dangers of investigational drugs often fail to account for the significant difference between risk assessments applied to the terminally ill and those applied to the average person. Terminally ill patients with no approved treatment options will likely die in a matter of months without further intervention. Treatment that is unreasonable for the average person may be quite reasonable where

¹⁴⁵ See Roberts et al., *supra* note 125, at 2130.

¹⁴⁶ See 21 C.F.R. § 312.23(a)(8) (2008).

¹⁴⁷ Susan Okie, *Access before Approval – A Right to Take Experimental Drugs?*, 355 NEW ENG. J. MED. 437, 439 (2006).

¹⁴⁸ *Id.*

¹⁴⁹ Jacobsen, *supra* note 20, at 206 (noting that this figure likely underestimates safety concerns) (citations omitted).

¹⁵⁰ *Id.*

imminent death is the alternative.¹⁵¹ Indeed, risk-benefit assessments and the reasonableness of treatment are largely subjective matters, and some studies demonstrate that patients facing a serious illness make very different assessments of the risks they are willing to confront compared to healthy individuals.¹⁵² For example, Slevin et al. found that patients with cancer were willing to undergo intensive chemotherapy with substantial adverse effects for a 1% chance of cure, compared to members of the general public, who indicated that they would require a 50% chance of cure to proceed with treatment in the same situation.¹⁵³ A regulatory policy that fails to account for this diverse set of preferences risks subordinating the welfare of the seriously and terminally ill to their healthier counterparts.¹⁵⁴

The Slevin et al. study supports the notion that the average person believes that accepting death and transitioning to palliative care is the most reasonable decision when facing slim odds of benefitting from an investigational drug. But insofar as this decision reflects a judgment about the value of quality of life, it overlooks the compatibility of focusing on quality of life through palliative care or symptom management and receiving treatment.¹⁵⁵ More importantly, pursuing treatment may actually improve quality of life regardless of its physical impact, and the risk-benefit assessment made by the average healthy person may be based on values that certain seriously and terminally ill patients do not share. In the words of Professor George Zimmer, a cancer victim and participant in several Phase I oncology trials:

Letting a patient choose the poisons (under professional guidance) adds something to the will to struggle. We who are struggling to escape cancer do not, obviously, want to die of it. . . . The enemy is not pain or even death, which will come for us in any eventuality. The enemy is cancer, and we want it defeated and destroyed. . . . This is how I want to die – not a

¹⁵¹ See Agrawal et al., *supra* note 12, at 1077 (stating that a slight chance of therapeutic benefit is not unreasonable for patients in whom all standard therapeutic interventions have failed).

¹⁵² See Agrawal et al., *supra* note 12, at 1078.

¹⁵³ *Id.* at 1077-1078 (citing Maurice L. Slevin et al., *Attitudes to Chemotherapy: Comparing Views of Patients with Cancer to Those of Doctors, Nurses, and General Public* 300 BRIT. MED. J. 1458 (1990)).

¹⁵⁴ Michael D. Greenberg, *Information, Paternalism, and Rational Decision-Making: The Balance of FDA New Drug Approval*, 13 ALB. L.J. SCI. & TECH. 663, 675 (2003).

¹⁵⁵ Agrawal et al., *supra* note 12, at 1077.

suicide and not passively accepting, but eagerly in the struggle.¹⁵⁶

The attitude expressed by Professor Zimmer supports the notion that there may be non-physical benefits to a decision to take an investigational drug. Especially for seriously and terminally ill patients, well-being goes beyond the mere absence of disease and includes psychological and social dimensions.¹⁵⁷ Data on the safety and effectiveness of investigational drugs fails to account for these non-physical dimensions.¹⁵⁸ Patients often seek out Phase I trials, even if chances of meaningful benefit are small, because their quality of life is improved by "not giving up."¹⁵⁹ Indeed, several studies have demonstrated that participating in Phase I oncology trials may improve patients' quality of life compared to the alternative of receiving supportive care.¹⁶⁰ For example, Melink et al. used Linear Analogue Self-Assessment (LASA), which is a self-reporting assessment tool that measures quality of life, to compare the quality of life of cancer patients who received a Phase I oncology treatment and cancer patients who were not eligible for a Phase I trial and who received supportive care.¹⁶¹ The results indicated that, while patients who received a Phase I oncology treatment did not report a significant change in quality of life after one course of therapy, patients who received supportive care reported a significant decrease in overall quality of life after a one month follow up.¹⁶² In addition, Berdel et al. used LASA to demonstrate that treatment with anticancer medication, both in a Phase I trial and outside of a clinical trial, had a significant positive influence on the psychological and social aspects of LASA,

¹⁵⁶ Christopher K. Daugherty et al., *Learning from Our Patients: One Participant's Impact on Clinical Trial Research and Informed Consent* 126 ANNALS INTERNAL MED. 892 (1997). See also Petition for Writ of Certiorari, *supra* note 13, at 14 ("Are the last days of a person's life better spent in painful struggle against nearly impossible odds, but with some hope and the conviction that she is doing everything possible? Or is it instead better or more noble to accept one's fate and spend the final days saying goodbye and hoping passively for a spontaneous remission? The patient's interest in weighing those values for herself transcends any disagreement about how to interpret the evidence from a particular clinical trial.").

¹⁵⁷ Agrawal et al., *supra* note 12, at 1076-77.

¹⁵⁸ *Id.* at 1077.

¹⁵⁹ Kurzrock et al., *supra* note 134, at 931.

¹⁶⁰ Agrawal et al., *supra* note 12, at 1077 (citing nine studies that demonstrate this result).

¹⁶¹ Teresa J. Melink et al., *The Impact of Phase I Clinical Trials on the Quality of Life of Patients with Cancer*, 3 ANTI-CANCER DRUGS 571, 571 (1992).

¹⁶² *Id.* at 573-75.

as indicated by feelings of well-being, mood, level of activity, and level of anxiety.¹⁶³

Although these considerations weaken the argument that FDA restrictions on access to investigational drugs protect the best interests of patients, the issue ultimately depends on whether serious and terminal illness or lack of information significantly undermine competence. Again, competent patients in collaboration with their physicians should be free to assume as much or as little risk as they choose. Some studies do present findings that correlate illness severity with compromised competence. For example, Schaeffer et al. found that illness severity had a negative effect on the amount of information retained in an informed consent document.¹⁶⁴ The study also found that even where the consent form indicated that the study was not designed for treatment, participants in Phase I trials enrolled primarily for treatment purposes.¹⁶⁵ The study concluded that Phase I and II subjects were more influenced by their own medical conditions, hope for control of disease, and perceived lack of any other choice, than by disclosed information.¹⁶⁶ Another study found that, although 90% of patients with cancer who participated in research reported being satisfied with the informed consent process, few understood the potential for incremental risk or discomfort from participating in research and the uncertainty of the benefits.¹⁶⁷ Results of this nature, however, are not uniform. For example, Casarett et al. used a Global Distress Index (GDI), which correlates with levels of distress in cancer patients, and found no relationship between GDI score and understanding of disclosed information or ability to reason through the risks and benefits of participating in a mock study.¹⁶⁸

More importantly, studies that appear to link illness severity with diminished decision-making capacity often fail to differentiate between comprehension – understanding the factual components of the information – and appreciation – what the information means to a

¹⁶³ Wolfgang E. Berdel et al., *Influence of Phase I Early Clinical Trials on the Quality of Life of Cancer Patients: A Pilot Study*, 8 ANTICANCER RES. 313 (1988).

¹⁶⁴ Monica Schaeffer et al., *The Impact of Disease Severity on the Informed Consent Process in Clinical Research*, 100 AM. J. MED. 261, 264 (1996).

¹⁶⁵ *Id.* at 266.

¹⁶⁶ *Id.*

¹⁶⁷ Agrawal et al., *supra* note 12, at 1078 (citing Steven Joffe et al., *Quality of Informed Consent in Cancer Clinical Trials: A Cross-Sectional Survey*, 358 LANCET 1772).

¹⁶⁸ David J. Casarett et al., *Identifying Ambulatory Cancer Patients at Risk of Impaired Capacity to Consent to Research*, 26 J. PAIN & SYMPTOM MGMT. 615, 619-20 (2003).

particular person.¹⁶⁹ Subjects may comprehend their limited chance of personal benefit and still hope that they will benefit.¹⁷⁰ Indeed, some studies indicate that subjects enrolled in Phase I trials hope that they will benefit, but understand that this outcome is unlikely.¹⁷¹ For example, Daugherty et al. found that possible therapeutic benefit motivated 85% of subjects to participate in a Phase I trial, but that 78% were either unwilling or unable to state whether they believed that they would personally benefit from participating.¹⁷²

The distinction between comprehension and appreciation also motivates a response to those who challenge competence based on the relatively small amount of information available about investigational drugs. Information is relevant to competence because of its effect on understanding, and generally persons understand if they "have acquired pertinent information and have justified, relevant beliefs about the nature and consequences of their actions."¹⁷³ The small amount of information available about a particular investigational drug may lead a patient to justifiably believe that the consequences of his or her decision to take the drug are not likely to be beneficial. But where accepting a serious disability or palliative care and a quiet death are inconsistent with the patient's values, deciding to take the drug anyway may be a perfectly competent, value-promoting decision. In other words, while the patient understands that the lack of information surrounding the drug makes benefit uncertain or unlikely, he or she appreciates the situation such that even a small chance of benefit is worth pursuing.

Furthermore, while many seriously or terminally ill patients may feel compelled by their circumstances to pursue treatment with an investigational drug, this compulsion is not coercion.¹⁷⁴ Coercion is a form of manipulation in which an agent intentionally narrows a person's options in an attempt to force the person to decide in a way that he or she would not otherwise decide.¹⁷⁵ For example, an armed thief coerces a victim to give up his or her wallet by narrowing the victim's options down to either giving up the wallet or getting shot. But when nature or accident narrows someone's options rather than intentional

¹⁶⁹ Agrawal et al., *supra* note 12, at 1079.

¹⁷⁰ *Id.* at 1080.

¹⁷¹ Kurzrock et al., *supra* note 134, at 931.

¹⁷² C. Daugherty et al., *Perceptions of Cancer Patients and Their Physicians Involved in Phase I Trials*, 13 J. CLINICAL ONCOLOGY 1062 (1995).

¹⁷³ Beauchamp et al., *supra* note 116, at 88.

¹⁷⁴ Agrawal et al., *supra* note 12, at 1081.

¹⁷⁵ See Hawkins et al., *supra* note 123, at 17.

action, the person simply suffers from bad luck.¹⁷⁶ Thus, unless someone contrives the situation, if a serious or terminal illness deprives a patient of valuable options to the extent that pursuing unproven treatment seems like the most reasonable decision, coercion is not an issue. Having few perceived options is entirely consistent with voluntary decision-making.¹⁷⁷ If critics of expanded access are claiming that the illness only makes pursuing unproven treatment *appear* to be the reasonable option when it is not actually so, then the problem is that the patient does not accurately understand the risks and benefits, which is a separate issue that does not involve coercion. Alternatively, the critic appreciates the situation differently and is implicitly making an unwarranted value judgment:

Claims of coercion [as a result of serious illness] may be projections rather than empirically substantiated facts. They arise from the view that any clearly thinking person would desire palliative care and being at home with family rather than aggressive chemotherapy at the end of life. But many dying people want chemotherapy, even if there is a very low chance of benefit and a reasonable chance of toxic effects, because it offers them hope or fits their life narrative to fight against the odds and to overcome challenges; to die without trying everything would be false to themselves and their values.¹⁷⁸

Indeed, citing the negative effects of serious and terminal illness on decision-making capacity results in a tension with the current practice of allowing seriously and terminally ill patients to participate in early-development drug research.¹⁷⁹ While the government requires researchers to protect all of their competent subjects by obtaining informed consent, it does not mandate any additional protection for the seriously and terminally ill, and the seriously and terminally ill are not listed as a vulnerable population by the Department of Health and Human Services in the Code of Federal Regulations.¹⁸⁰

Finally, the gatekeeping role of the medical profession further undermines the argument that FDA restrictions on access to investigational drugs are necessary to protect the best interests of seriously and

¹⁷⁶ See *id.* (stating that coercion requires the intentional limiting of a persons options in an attempt to manipulate her).

¹⁷⁷ Agrawal et al., *supra* note 12, at 1081.

¹⁷⁸ *Id.*

¹⁷⁹ See Robertson, *supra* note 20, at 17.

¹⁸⁰ See 45 C.F.R. § 46.111(a)(3) (2008) (listing children, prisoners, pregnant women, mentally disabled persons, and economically or educationally disadvantaged persons as vulnerable populations).

terminally ill patients. Patients will of course only be able to obtain these drugs in consultation with their physician, and physicians have a professional obligation not to pursue treatment that they believe will harm their patient. In fact, with personal and direct knowledge of the patient's condition and circumstances, physicians may be in a better position to assess the risks to the patient posed by an investigational drug than the FDA. With the medical profession already in place as a mediator and safety valve situated between patients and investigational drugs, the FDA's role as protector of patients in this context risks becoming overprotective. When also considering that investigational drugs are increasingly effective and not exceedingly unsafe for seriously and terminally ill patients with no approved treatment options and that challenges to the competence of a seriously or terminally ill patient's decision to take an unapproved drug are overstated or flawed, justifying the FDA's restrictions on access by appealing to the best interests of seriously and terminally ill patients begins to resemble strong paternalism.

B. Regulating Investigational Drugs to Promote Public Health

The primary public health objection to expanding access to investigational drugs stems from the public health benefit received from efficient clinical trials and the potential for expanded access to undermine these trials. A fast, effective system of clinical trials ensures that beneficial drugs reach the public as quickly as possible and that harmful drugs never reach the public. Expanded access threatens to undermine clinical trials in two ways. First, as the HDC-ABMT case illustrates,¹⁸¹ providing investigational drugs for treatment use can negatively affect trial enrollment because patients have little incentive to enroll in a trial in which they may receive a placebo when they can obtain investigational drugs in a treatment setting.¹⁸² In turn, prolonged clinical trials delay the benefits of safe and effective drugs to future patients and the public. The second way in which expanded access may undermine clinical trials relates specifically to the prospect of allowing drug companies to charge a profit-making price for investigational drugs. Namely, doing so could reduce the incentive to complete the rigorous clinical trial process by making it more attractive to sell unapproved drugs than to diligently pursue full market

¹⁸¹ See *supra* Section I (describing the HDC-ABMT case).

¹⁸² See Corrected *En Banc* Brief for the Appellees, *supra* note 87, at 11; Jacobsen, *supra* note 20, at 206-07; Okie, *supra* note 147, at 437; Benderly, *supra* note 93, at 4.

approval.¹⁸³ The resulting delays in clinical trials would ultimately harm the public.

Furthermore, allowing drug companies to charge a profit-making price for investigational drugs could have the additional negative effect on public health of widening existing health disparities. Both public and private health insurance would almost certainly not cover the vast majority of investigational drugs. Insurance plans exclude “experimental” or “investigational” treatments in a variety of ways.¹⁸⁴ Some policies leave the determination up to the plan administrator, while others exclude treatments under “clinical investigation,” treatments “not generally recognized by the medical profession as tested and accepted medical practice,” or treatments “still requiring future approval by the Federal Drug Administration or other governmental agency.”¹⁸⁵ These exclusionary clauses are often desirable from the standpoint of economic utility and cost containment.¹⁸⁶ Plan administrators have a limited amount of funds to provide for the medical needs of plan members, and resources should arguably only be used to pay for treatments proven to be safe and effective.¹⁸⁷ Although increasing premiums to cover costs is an option, the increase required to begin covering investigational drugs would likely make health insurance unaffordable for some and an undue burden for many others. Thus, insurance would not and should not cover the majority of investigational drugs, which would force patients to pay for these drugs out-of-pocket. Because many patients in need would likely be unable to afford these drugs, the unjust and already wide health disparities between the rich and the poor¹⁸⁸ may widen further as a result.

As an initial matter, it is worth noting that the public health benefits of maintaining the integrity of clinical trials largely do not apply to patients who are currently terminally ill and who have no approved treatment options. Because the clinical trials process takes an average

¹⁸³ Corrected *En Banc* Brief for the Appellees, *supra* note 87, at 11, 15, 57.

¹⁸⁴ Sharona Hoffman, *A Proposal for Federal Legislation to Address Health Insurance Coverage for Experimental and Investigational Treatments*, 78 OR. L. REV. 203, 208 (1999).

¹⁸⁵ *Id.* (citations omitted).

¹⁸⁶ *See id.* at 210.

¹⁸⁷ *Id.* at 210-11.

¹⁸⁸ *See e.g.*, U.S. CENSUS BUREAU, INCOME, POVERTY, AND HEALTH INSURANCE COVERAGE IN THE UNITED STATES: 2006 21 (2007), available at <http://www.census.gov/prod/2007pubs/p60-233.pdf> (indicating that the likelihood of lacking health insurance increases with declining income, with 24.2% of people with a yearly income less than \$25,000 being uninsured in 2006, compared to 7.7% of people with a yearly income of \$75,000 or more).

of seven years to complete,¹⁸⁹ these patients likely will not live long enough to experience the benefits of clinical trials. If FDA regulations are indeed strongly paternalistic towards the terminally ill, then the public health benefits of FDA restrictions on access burden this population in order to benefit the public. Although such utilitarian based public health policies are commendable in certain cases,¹⁹⁰ if there is any way to reduce the burden on the negatively affected population without jeopardizing public health, policymakers should take these steps. Otherwise, the regulations are overbroad. Because policymakers *can* create more tailored legislation that eases the restrictions on access to investigational drugs *without* significantly jeopardizing public health, my responses to the public health objections to expanding access are also the basis of my recommendations for legislation.

V. RECOMMENDATIONS FOR LEGISLATION

A. Allow Drug Sponsors to Conditionally Charge a Profit-Making Price for Investigational Drugs for Treatment Use

Most significantly, Congress should amend the FDCA to require the FDA to allow IND sponsors to charge a profit-making price for investigational drugs for treatment use.¹⁹¹ Doing so would remove the most substantial disincentive to industry participation in expanded access programs. This ability to profit, however, should be conditioned on three qualifications. First, recognizing that allowing profit could put drug companies in a position to exploit the seriously and terminally ill, legislation should prohibit price gouging in the context of expanded access programs.¹⁹² Most states prohibit all industries from engaging in price gouging during a state of emergency.¹⁹³ Insofar as a serious or terminal illness is an individual emergency, Con-

¹⁸⁹ Groopman, *supra* note 14, at 2.

¹⁹⁰ E.g. requiring the involuntary quarantine of anyone with a highly contagious and serious disease.

¹⁹¹ The FDA should retain the authority to prohibit IND sponsors from charging a profit-making price for investigational drugs in a clinical trial setting.

¹⁹² See Section IV.A.1 for a description of price gouging ("[p]rice gouging occurs when a seller takes advantage of an unusually high demand and lack of competition by charging excessively high prices.").

¹⁹³ See Nat'l Conference of State Legislatures, Prescription Drug Safety: Emergency Controls, Scams and Long-Distance Sales, <http://www.ncsl.org/programs/health/Rxemerg.htm> (last visited Sept. 26, 2008) (quoting the provisions of laws from twenty-five different states that prohibit price gouging during an emergency).

gress, by analogy, should apply similar provisions at the federal level to drug companies selling investigational drugs. For example, Congress could prohibit drug companies from charging a price for an investigational drug that is more than 20% above the market price of a reasonably comparable approved drug. Second, legislation should prevent exploitation of the seriously and terminally ill by restricting the marketing of investigational drugs more than the marketing of prescription drugs. Congress should prohibit direct-to-consumer advertising of investigational drugs and require the FDA to establish stringent guidelines for advertisements directed towards physicians.

Third, in order to counteract the risk that profiting from investigational drugs will delay marketing approval, profit should be conditional on evidence that the drug sponsor is continuing to diligently pursue clinical trials. Legislation should leave the task of how to accomplish this up to the FDA, which has expertise in the area of drug regulation. The FDA should use its delegated authority to set forth specific requirements to ensure that companies that profit in this context continue to diligently pursue clinical trials for the investigational drug being sold. For example, the FDA could require sponsors who wish to sell investigational drugs for profit to submit a copy of their general investigational plan, including a development timeline and enrollment estimates.¹⁹⁴ The FDA could then periodically monitor progress to ensure that actual development and enrollment estimates are not significantly behind or less than the original projections.¹⁹⁵ If development appears delayed, the FDA could require a compelling justification for the delay. If the sponsor does not provide a compelling justification, the FDA could temporarily or permanently revoke the drug's IND status under its existing authority.¹⁹⁶

One objection to conditionally allowing drug sponsors to profit from investigational drugs is that doing so is susceptible to abuse considering the difficulty and the monitoring burdens associated with ensuring that sponsors do not delay marketing approval. Indeed, a rule that outright prohibits sponsors from charging a profit-making price might be reasonable if delaying or abandoning attempts at full market approval in favor of selling investigational drugs were a viable business model. However, there are substantial financial and logistical concerns that militate against widespread industry participation in

¹⁹⁴ See Nat'l Patient Advocate Found., A Written Comment Submitted to the FDA (Mar. 14, 2007), <http://www.fda.gov/ohrms/dockets/DOCKETS/06n0062/06n-0062-EC90-Attach-1.pdf>.

¹⁹⁵ See *id.*

¹⁹⁶ See 21 C.F.R. § 312.44 (2008) (describing the conditions under which the FDA may terminate an IND).

a post-Phase I market.¹⁹⁷ For example, the market for investigational drugs would be relatively small: seriously and terminally ill patients who have exhausted all approved treatment options.¹⁹⁸ More importantly, drug companies often have a very limited drug supply early in development.¹⁹⁹ Where there is little evidence that an investigational drug will be safe and effective and therefore valuable on the full market, the incentive to undertake the substantial investment needed to produce larger quantities of drugs in the early stages of development simply may not exist.²⁰⁰

In turn, this conclusion supports three further conclusions: allowing drug companies to charge a profit-making price for investigational drugs 1) will not substantially expand access early in the testing process; 2) will not significantly harm the public by removing the incentive to pursue clinical trials; 3) will be more likely to prompt drug manufacturers to produce larger quantities of investigational drugs and expand access where results from early clinical trials are promising. Although the first conclusion in part undermines the purpose of allowing drug companies to profit in this context, the second conclusion illustrates that prohibiting these profits is an unnecessary disincentive that burdens the few patients who would otherwise obtain access early in the testing process. Moreover, the third conclusion means that patients will be more likely to obtain access to beneficial investigational drugs and less likely to obtain access to harmful investigational drugs. More specifically, the profit motive may only induce drug sponsors to produce enough drugs to expand access where the sponsor calculates that the drug is likely to receive full market approval because of favorable early test results. The drugs that are more likely to receive market approval are also more likely to be safe and effective. Essentially, along with the medical profession, the market would act as a mediator and safety valve situated between patients and investigational drugs. Thus, conditioning a drug spon-

¹⁹⁷ Currie, *supra* note 81, at 322.

¹⁹⁸ The requirement that eligible patients be unable to enter into a clinical trial, discussed in Section V:B, *infra*, would reduce the size of this market even further.

¹⁹⁹ Currie, *supra* note 81, at 322.

²⁰⁰ See *id.* (stating that the economies of scale needed to prompt manufacturers to produce larger quantities of drugs may not exist in the early stages of development); Robertson, *supra* note 20, at 17 (stating that selling drugs outside Phase II trials would not be a viable business model for most companies); Groopman, *supra* note 14, at 6 (quoting Richard Merrill, a professor at the University of Virginia Law School and a prominent expert on drug regulation, for the proposition that the right sought by the Abigail Alliance in *Abigail Alliance v. Eschenbach* would require a major investment to scale up production).

sor's ability to profit from investigational drugs on requirements not to neglect full market approval, engage in price gouging, or use manipulative marketing techniques is a feasible way to expand access without harming patients or jeopardizing public health.

B. Prohibit Patients Who Can Enter into a Clinical Trial from Obtaining the Requested Investigational Drug

Congress should also amend the FDCA to prohibit patients who are able to enter into a clinical trial for the requested investigational drug from obtaining it for treatment use.²⁰¹ This will ensure that providing investigational drugs for treatment use does not delay the clinical trial process by diverting potential trial participants. If a patient does not qualify for a particular trial because of the nature of his or her condition or treatment history, because the trial is already full, or because the location of the trial makes participation impractical, allowing the patient to access the investigational drug being tested will not significantly threaten clinical trial enrollment and thus will do little to undermine the testing process. Again, Congress should rely on the FDA's discretion regarding how to implement this requirement. For example, the FDA could review its clinical trial database to ensure that patients seeking investigational drugs cannot qualify for a clinical trial for the requested drug or a clinical trial is not geographically accessible. If the patient were unable to enter into a clinical trial, the FDA would not intervene in the transaction between the drug company and the patient. If the patient were able to enter into a clinical trial, the FDA would prohibit the transaction and inform the patient's physician of the available trial. Delegating the responsibility of reviewing available clinical trials to the FDA rather than the physician will prevent physicians from encountering an additional administrative burden in the expanded access process. In addition, the FDA may have access to information about clinical trials that physicians and the public do not.²⁰²

²⁰¹ Requiring seriously and terminally ill patients without approved treatment options who are seeking an investigational drug for treatment use to enter into a randomized clinical trial where they may receive a placebo potentially raises ethical concerns. Addressing these concerns, including the scientific value of placebo controls in comparison to alternatives such as historical controls, is beyond the scope of this paper.

²⁰² See Statement by Richard Pazdur, M.D., Director, Division of Oncology Drug Products, Food and Drug Administration, Department of Health and Human Services Before the H. Comm. on Government Reform, 106th Cong. (2000), available at <http://www.fda.gov/ola/2000/cancerdrugs.html> (stating that strict rules of confidentiality bind the FDA concerning the information it can disclose to a physician about

C. Encourage Drug Companies to Allocate Promising Investigational Drugs to Indigent Drug Programs

Recognizing that regulations that allow drug companies to profit from investigational drugs could increase health disparities due to lack of insurance coverage, legislation should encourage drug sponsors to start allocating a certain amount of their more promising investigational drugs to indigent drug programs. Many drug companies pay to provide a fixed amount of certain approved drugs to indigent patients in the hope that the resulting improved image will ultimately influence prescription patterns.²⁰³ Company representatives undoubtedly limit the supply of drugs in these programs to ensure that the costs are more than covered by cost-shifting and the profits from selling drugs to able payers.²⁰⁴ If drug companies offered some of their more promising investigational drugs through these programs, patients who are below a certain poverty level and who otherwise meet all of the expanded access requirements could obtain these drugs. Although simply encouraging drug companies to participate may seem like an empty provision, highlighting awareness of the issue could help create an environment in which drug companies have a greater self-promotion incentive to finance the treatment use of certain investigational drugs. Admittedly, this proposal may seem like a step back towards the original problem created by prohibiting drug companies from profiting in this context. However, allowing companies to profit from those who *can* afford investigational drugs may make companies more willing to finance limited access for those who *cannot* afford these drugs.

But this may not be a satisfactory response to the problem of widening health disparities. First, it is simply weak: encouraging drug companies to provide free drugs is far from an assurance that they will do so. Second, the indigent are not likely to be well educated and thus are more likely to be ill equipped to understand the risks of investigational drugs. Adding to the problem, the indigent typically have less access to health care,²⁰⁵ so that providing them with investigational drugs outside of a controlled clinical trial environment could create significant safety and monitoring concerns. When it comes to

the sponsor's product and development data).

²⁰³ Telephone Interview with Michael Winniford, *supra* note 11. See also *supra* Section IV.A (describing the self-promotion incentive to participate in expanded access programs).

²⁰⁴ Telephone Interview with Michael Winniford, *supra* note 11.

²⁰⁵ See U.S. CENSUS BUREAU, *supra* note 188, at 21 (indicating that persons with lower income are less likely to be covered by health insurance than persons with higher income).

indigent patients, the medical profession may not be a reliable mediator between patients and investigational drugs.

Although there is no perfect response to the risks created by providing investigational drugs to the indigent, the market may once again mitigate some of the risk. To ensure that the maximum amount of physicians are aware of drug companies providing free drugs, companies typically only allocate high-demand drugs to their indigent drug programs.²⁰⁶ While there are exceptions to every rule, high-demand drugs tend to be relatively safe and effective drugs. Thus, the investigational drugs provided to indigent patients would likely be safe and effective compared to other investigational drugs. At the very least, this mitigates some of the safety concerns related to providing these drugs to indigent patients.

There are two responses to the claim that encouraging drug companies to allocate investigational drugs to their indigent drug programs is too weak as a solution to the problem created by increased health disparities. First, any increase in health disparities would likely be small, corresponding to the relatively small market for investigational drugs: terminally and seriously ill patients with no FDA approved treatment options. Requiring that eligible patients be unable to enter into a clinical trial would reduce the size of this market even further. Second, the entire objection relating to inequitable access assumes that widening health disparities as a result of increasing the supply of a potential medical benefit is unacceptable policy. Alternatively, some might argue that the fewer who are unjustly denied a potential medical benefit the better. According to this argument, expanding access is better than not doing so, even where the resulting access is inequitable. This argument is especially plausible in the context of medical treatments, such as investigational drugs, as opposed to enhancements, such as cosmetic surgery. As regrettable as the situation is, many would not accept the notion that the relatively well-off should not have access to potentially life-saving or life-extending treatments solely because some patients cannot afford these treatments. In any event, even for those who do accept this notion, encouraging drug companies to provide promising investigational drugs in their indigent drug programs could help reduce the relatively small increase in health disparities that would result from allowing companies to profit.

²⁰⁶ *Id.*

D. Reduce Disincentives Related to Liability,
Data Collection and Administrative Burdens

Finally, legislation should contain provisions that reduce the disincentives to providing investigational drugs for treatment use related to liability, data collection, and the administrative burden on physicians.²⁰⁷ Insofar as informed consent is not sufficient legal protection,²⁰⁸ Congress should explicitly permit patients who meet the criteria for an expanded access protocol to waive their right to sue drug sponsors for an adverse outcome caused by an investigational drug. State governments already allow similar waivers in other contexts. For example, in Ohio, proprietors of potentially dangerous recreational activities such as auto racing and horseback riding can require participants to waive the proprietor's liability for negligent conduct, but not wanton or willful misconduct.²⁰⁹ Similarly, Congress should permit patients to waive drug sponsors liability for negligence for an adverse outcome caused by an investigational drug, but not for intentional misconduct. This is a fair way to allow patients to assume the risk of engaging in a relatively unsafe practice and to remove a disincentive to sponsors providing access at the same time. In many cases, the knowledge that waiving this right will increase a sponsor's willingness to cooperate will lead the patient to sign a waiver. But in the interest of preserving patient autonomy, even if nominal in some cases, legislation should not require this waiver.

Regarding disincentives related to data collection, legislation should require the FDA to account for safety and efficacy information from expanded access protocols when patients are within the scope of the intended use of the drug.²¹⁰ While not as reliable as data from controlled studies, knowing that a drug helps the kinds of severely ill patients who are generally excluded from clinical trials could enable a sponsor to obtain broader FDA approval and substantially increase revenues.²¹¹ Congress should leave the decision how to specifically incorporate this data into a New Drug Application to the FDA's discretion.

Lastly, Congress should attempt to ease some of the administrative burdens on physicians by making the clinical trials process as

²⁰⁷ See *supra* Section III.B (describing the disincentives to making investigational drugs available for treatment use).

²⁰⁸ See Talbott, *supra* note 98, at 318.

²⁰⁹ Bishop v. Nelson Ledges Quarry Park, No. 2004-P-0008, 2005 WL 1272299, at *4 (Ohio Ct. App. May 27, 2005) (citations omitted).

²¹⁰ GLAXOSMITHKLINE, *supra* note 95.

²¹¹ See Groopman, *supra* note 14, at 7.

transparent and accessible as possible. Policymakers should pass legislation such as the Fair Access to Clinical Trials Act of 2007 (FACT Act),²¹² or incorporate its provisions into new legislation. The FACT Act, which is currently before the 110th Congress,²¹³ mandates registration of all clinical trials conducted in the United States on ClinicalTrials.gov, requires investigators to report details such as research outcomes, significant adverse events, and FDA approval status, and establishes enforcement mechanisms such as financial penalties and preclusion from Institutional Review Board approval for failure to comply.²¹⁴ By consolidating clinical trial information into a single accessible and convenient source and establishing enforcement mechanisms, the FACT Act would make it easier for physicians to find and research appropriate investigational drugs for their patients and to request information from the sponsor.²¹⁵

E. Summary of Recommendations

Implementing these recommendations will eliminate the elements of strong paternalism in the current regulations by easing restrictions on access to investigational drugs and will do so without significantly jeopardizing patient safety or public health. Allowing drug sponsors to charge a profit-making price for investigational drugs will remove a substantial disincentive to access that afflicts the current system. Conditioning this ability to profit on requirements not to neglect full market approval, engage in price gouging, or use manipulative marketing techniques will protect patients from exploitation and ensure that the public receives the full benefits of clinical trials. Prohibiting patients who are able to enter into a clinical trial from obtaining the relevant investigational drug for treatment use will ensure that expanding access does not delay the clinical trial process by diverting potential trial participants. Taking these steps while encouraging drug companies to allocate promising investigational drugs to their indigent drug programs will help reduce the relatively small increase in health disparities that may result from allowing profit in this context.

²¹² Fair Access to Clinical Trials Act of 2007, S. 467, 110th Cong. (2007).

²¹³ *See id.*

²¹⁴ Gold & Studdert, *supra* note 102, at 816.

²¹⁵ Under the current system, there is substantial evidence that researchers often do not submit studies with poor outcomes for publication, which skews systematic clinical trial reviews and meta-analyses that clinicians and policymakers use to guide health care policy. *Id.* Requiring researchers to publish data from *all* clinical trials has the additional benefit of helping to eliminate this “positive publication bias.” *Id.* at 812.

Finally, removing disincentives to industry involvement in expanded access programs related to drug sponsor liability, data collection, and administrative burdens on physicians will further expand access without significantly compromising patient safety or public health.

VI. THE ACCESS ACT

In limited respects, the Access, Compassion, Care, and Ethics for Seriously Ill Patients Act (ACCESS Act) approximates the ideal for regulating investigational drugs for treatment use.²¹⁶ Republican Sam Brownback introduced the ACCESS Act into the Senate in November 2005²¹⁷ and reintroduced it in May 2008,²¹⁸ while Republican Christopher Shays introduced it into the House of Representatives in October 2006²¹⁹ and Democrat Diane Watson reintroduced it in June 2008.²²⁰ Although the bill died in committee on every occasion, it is worth evaluating due to its apparent ability to resurface as the congressional standard for expanded access legislation.²²¹

The ACCESS Act establishes a three-tiered approval mechanism for new drugs that coexists with the current FDA framework for drug approval.²²² Tier I approval means that drugs are no longer fully “investigational,” but “approved” for sale on a restricted market, profits included.²²³ In order to receive Tier I approval, sponsors must

²¹⁶ See Access, Compassion, Care, and Ethics for Seriously Ill Patients Act, S. 1956, 109th Cong. (2005).

²¹⁷ ACCESS Act, S. 1956, 109th Cong. (2005), <http://www.govtrack.us/congress/bill.xpd?bill=s109-1956> (last visited Oct. 5, 2008).

²¹⁸ ACCESS Act, S. 3046, 110th Cong. (2008), <http://www.govtrack.us/congress/bill.xpd?bill=s110-3046> (last visited Jan. 27, 2009).

²¹⁹ ACCESS Act, H.R. 6303, 109th Cong. (2006), <http://www.govtrack.us/congress/bill.xpd?bill=h109-6303> (last visited Oct. 5, 2008).

²²⁰ ACCESS Act, H.R. 6270, 110th Cong. (2008), <http://www.govtrack.us/congress/bill.xpd?bill=h110-6270> (last visited Jan. 27, 2009).

²²¹ The ACCESS Act as reintroduced in the 110th Congress was similar, but not identical to the ACCESS Act as introduced in the 109th Congress. See Kurt Karst, *ACCESS Act Reintroduced by Sen. Brownback; Previous Tiered Approval Nomenclature Scrapped and New Immunity Provision Added*, FDA Law Blog, June 4, 2008, http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2008/06/access-act-rein.html. Because of the time at which this note was written, I only address the version introduced in the 109th Congress.

²²² See Groopman, *supra* note 14, at 5.

²²³ See Access, Compassion, Care, and Ethics for Seriously Ill Patients Act, S. 1956, 109th Cong. § 5(h)(3) (2005) (referring to Tier I approval for marketing); *id.* at § 5(f) (directing the FDA to establish a new expanded access program for investigational drugs apart from the tiered approval program, which indicates that tiered approval is a form of market approval). See also Ryan, *supra* note 92 (interviewing Frank Burroughs, founder of the Abigail Alliance for Better Access to Developmental Drugs, who juxtaposes the Abigail Alliance’s Tier I approval proposal, the predeces-

submit an application to the Secretary of Health and Human Services containing: 1) data from Phase I clinical trials, 2) evidence based on data such as case histories, data from animal and computer models, information about the pharmacological mechanism of action, or comparison with historical data, and 3) an assurance that the sponsor will continue clinical investigation to obtain full market approval.²²⁴ The Secretary must approve the application if the risk of the disease outweighs the risk of the drug for a patient subpopulation, and the drug may benefit patients in this subpopulation.²²⁵

In addition, the bill requires the labels on Tier I drugs to state that 1) the drug is intended for use by a patient whose physician has documented that the patient has exhausted all approved treatment options; 2) the drug is intended for use by a patient whose physician has documented that the patient “unsuccessfully sought treatment, or obtained treatment that was not effective, with an investigational drug, biological product, or device for which such individual is a reasonable candidate”; 3) every patient who receives the drug shall provide a waiver of the right to sue the drug sponsor or the prescribing physician; and 4) every patient who receives the drug shall allow the sponsor to obtain data about the patient that may be used to support Tier II or III approval.²²⁶

Although the ACCESS Act takes a commendable step towards expanding access, it contains some significant flaws. For instance, the requirements that an eligible patient must have exhausted approved treatment options and unsuccessfully sought treatment with an investigational drug are simply labeling requirements with no meaningful enforcement mechanisms.²²⁷ By contrast, under the current expanded access system, the FDA verifies that the patient meets the necessary requirements before allowing a transaction between an investigational drug sponsor and a patient to occur.²²⁸ In part, this difference exists because the ACCESS Act approves drugs for an entire market rather than for individual patients or groups of patients as occurs under the current system. The market would only be restricted insofar as patients and physicians complied with certain labeling requirements. While this would undoubtedly reduce administrative burdens and time

sor to the ACCESS Act, to the current Treatment IND system by stating that Tier I allows drug companies to “charge” for the drug, rather than merely recovering costs under a Treatment IND).

²²⁴ S. 1956 § 3(a)-(b).

²²⁵ See *id.* at § 3(b)(4).

²²⁶ *Id.* at § 3(b)(5).

²²⁷ See *id.*

²²⁸ See 21 C.F.R. § 312.34(a)-(c) (2008).

delays, it is also susceptible to abuse in that it would conceivably be easy for a patient who has not actually met these labeling requirements to obtain the drug. This potential for abuse undermines the public health and patient safety concerns that motivate the labeling requirements.

Moreover, the labeling requirement that the patient must have unsuccessfully sought treatment with an investigational drug does not explicitly mention clinical trials.²²⁹ It is thus too ambiguous to approximate the requirement that the patient must be unable to enter into a clinical trial for the relevant drug. Also ripe for abuse, the requirement that the sponsor continue to pursue full market approval following Tier I approval simply calls for an "assurance" that the sponsor will do so.²³⁰ The bill does not describe any procedures for establishing compliance, and does not direct any administrative agency to do so.²³¹ Thus, although the ACCESS Act takes steps towards expanding access to investigational drugs, it ultimately does not adequately protect the government's interests in protecting patient best interests and promoting public health.

VII. CONCLUSION

In the Food and Drug Administration Modernization Act of 1997, Congress instructed the FDA to ensure that "opportunities to participate in expanded access programs are available to every individual with life threatening or serious debilitating illness for which there is not effective therapy."²³² Eleven years later, the FDA has failed to accomplish this goal. What is more, the government's interest in protecting patients from their own decision to take an investigational drug does not justify the extent of the FDA's restrictions on access. Because courts are not likely to establish a constitutional right to freedom from government interference with the pursuit of investigational medical treatment following *Abigail Alliance v. Eschenbach*, proponents of expanded access must pursue reform through Congress, which should direct the FDA to reform its overbroad regulations. By implementing the legislative and regulatory recommendations presented here, Congress and the FDA can ease the strongly paternalistic restrictions on access to investigational drugs without significantly jeopardizing patient safety or public health.

²²⁹ See S. 1956 § 3(b)(5)(A)(i).

²³⁰ See *id.* at § 3(b)(1)(A)(iii).

²³¹ See *id.* at § 1-7.

²³² See Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75147, 75149 (Dec. 14, 2006).